

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**



GR

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :  A61K 7/48, 7/50		A1	(11) International Publication Number: WO 97/47171  (43) International Publication Date: 18 December 1997 (18.12.97)
<p>(21) International Application Number: PCT/EP97/02984</p> <p>(22) International Filing Date: 5 June 1997 (05.06.97)</p> <p>(30) Priority Data: 9612067.0                    10 June 1996 (10.06.96)                    GB</p> <p>(71) Applicant (<i>for all designated States except US</i>): SMITHKLINE BEECHAM PLC [GB/GB]; New Horizons Court, Brentford, Middlesex TW8 9EP (GB).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (<i>for US only</i>): CHARLTON, Lynda, Rosemary [GB/GB]; SmithKline Beecham Consumer Healthcare, St. George's Avenue, Weybridge, Surrey KT13 0DE (GB). MCGILLYCUDDY, Juliet, Teresa [IE/GB]; SmithKline Beecham Consumer Healthcare, St. George's Avenue, Weybridge, Surrey KT13 0DE (GB). OWEN, Sharon [GB/GB]; SmithKline Beecham Consumer Healthcare, St. George's Avenue, Weybridge, Surrey KT13 0DE (GB).</p> <p>(74) Agent: WHITE, Susan, Mary; SmithKline Beecham plc, Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b>  <i>With international search report.</i>  <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>	
<p>(54) Title: SKIN WASH COMPOSITION</p> <p>(57) Abstract</p> <p>A skin wash composition intended for topical application to water-wetted skin comprising an <math>\alpha</math>-hydroxy acid active ingredient formulated in a mild and non-irritant detergent base consisting of a mixture of a non-ionic alkylpolyglucoside surfactant and an amphoteric surfactant.</p>			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LJ	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

## SKIN WASH COMPOSITION

The present invention relates to compositions for topical application to the skin surface, in particular to skin wash compositions which are applied to water-wetted skin and subsequently rinsed off with water. Specifically, the present invention relates to skin wash compositions comprising an  $\alpha$ -hydroxy acid and other acids as defined herein as an active ingredient formulated in a mild and non-irritant detergent base.

Compounds generally known in the field of cosmetic and therapeutic skin treatments as  $\alpha$ -hydroxy acids and other acids as defined herein include compounds such as salicylic acid, lactic acid and glycolic acid. These compounds constitute the active ingredients of a number of commercially available products which are applied to the skin in order to confer a beneficial effect with respect to appearance and skin condition, in particular smoothness and suppleness. Salicylic acid for example has been shown to have keratolytic and comedolytic activity as well as anti-bacterial efficacy and has been used in the treatment and prevention of mild to moderate acne for more than 100 years. Lactic acid has a beneficial effect on skin hydration and is a constituent of a number of skin tonic and moisturising products.

**20**  $\alpha$ -Hydroxy acids and other acids as defined herein, whilst conferring a beneficial effect on the skin, may cause local irritation when applied to sensitive areas of the skin, in particular the face. Moreover, local irritation may be exacerbated by the carrier system in which the active ingredient is formulated. For example, skin wash compositions and in particular face wash compositions which are generally formulated with a soap-free detergent base selected for effective cleansing and foaming, may confer an irritant effect due to the use of ionic surfactants commonly employed in such detergent systems.

A further problem associated with formulating compositions containing  $\alpha$ -hydroxy acids and other acids as defined herein arises because of the desirability to formulate the composition at an acid pH at which the most efficacious free-acid form of the acid will predominate. For skin wash compositions, this problem is exacerbated by the

difficulty of obtaining a detergent base system at sufficiently low pH. A skin wash composition described as having a gentle yet effective cleanser for acne treatment and containing 2.0% w/w salicylic acid in a detergent base comprising a mixture of anionic and amphoteric surfactants is commercially available. Analysis of this

5 product, shows that it has a pH of 5. It follows, having regard to the pKa of salicylic acid which is attributed the value 2.97, that the free-acid form of the hydroxy acid does not predominate in this product and that its efficacy is accordingly not fully optimised.

10 It is an object of the present invention to provide a skin wash composition containing an  $\alpha$ -hydroxy acid or other acid as defined herein and a detergent base which has good cleansing and foaming characteristics, is mild and non-irritant and wherein the pH of the composition approaches the pKa of the acid such that the efficacy of the acid is enhanced. This object is achieved according to the present invention which is based

15 on the unexpected finding that a detergent base comprising a mixture of a non-ionic alkylpolyglucoside surfactant and an amphoteric surfactant not only has the desired cleansing and foaming characteristics and is mild and non-irritant when applied to the skin but also enables compositions to be formulated at low pH.

20 According to the present invention there is provided a skin wash composition comprising from 0.1 to 10 %w/w of an  $\alpha$ -hydroxy acid or other acid as defined herein and a detergent base consisting of a mixture of a non-ionic alkylpolyglucoside surfactant and an amphoteric surfactant wherein the pH of the composition is in the range 3.0 to 4.5.

25 Suitable acids for incorporation into skin wash compositions of the invention include salicylic acid, lactic acid, citric acid, glycolic acid, malic acid, maleic acid, pyruvic acid and hydroxy-octanoic acid. Preferred acids are salicylic acid, lactic acid and glycolic acid, especially salicylic acid and lactic acid. Salicylic acid will suitably be

30 present in compositions of the invention at a concentration in the range 0.2 to 5.0% w/w, more suitably in the range 1.0 to 3.0% w/w. A preferred concentration for

salicylic acid is 2.0 %w/w. Lactic acid will suitably be present in compositions of the invention at a concentration in the range 0.1 to 5.0 %w/w, more suitably in the range 0.5 to 2.5 %w/w. A preferred concentration for lactic acid is 1 %w/w. Glycolic acid will suitably be present at a concentration in the range 2.0 to 10.0 %w/w.

5

As used herein, the term alkylpolyglucoside surfactant means a non-ionic surfactant derived from common natural organic monomer units as found in starch, fats and sugars, and most suitably derived from D-glucose monomer units.

Alkylpolyglucosides derived from D-glucose are acetal compounds in which the alkyl residue has a carbon chain length of from 8 to 16 carbon atoms and the degree of glucosidation (or polymerisation), ie. the average number of glucose units per alkyl radical, is between 1.1 and 6. A range of suitable alkylpolyglucosides are commercially available either individually or as mixtures or blends. Compositions according to this invention will generally contain mixtures or blends of different alkylpolyglucosides. Preferred alkylpolyglucosides for use in the present invention include decyl glucoside and lauryl glucoside and mixtures thereof.

Alkylpolyglucoside surfactants generally comprise up to 20 %w/w of the skin wash composition, suitably from 2.0 to 15.0 %w/w and preferably from 4.0 to 10.0 %w/w of the composition. It will be appreciated that the amount of alkylpolyglucoside will be determined to some extent by the nature and amount of amphoteric surfactant present in the composition.

In principle, any amphoteric surfactant which is acceptable for topical application to the skin may contribute, with the alkylpolyglucoside surfactant, to the detergent base but, in view of their inherent mildness and good foaming performance, the preferred amphoteric surfactant will belong to the class of compounds known as betaines. Structurally, betaine compounds contain a carboxylate functional group and a quaternary nitrogen function separated by a methylene moiety. They include n-alkyl betaines such as cetyl betaine and behenyl betaine, and n-alkylamido betaines such as cocoamidopropyl betaine. The amphoteric surfactant component of the detergent base for compositions of the present invention may be a single compound or a mixture of

blend of two or more different substances. A preferred amphoteric surfactant is cocoamidopropyl betaine. Amphoteric surfactants will generally comprise up to 10 %w/w of the skin wash composition, suitably from 2.0 to 8.0 %w/w and preferably from 2.5 to 6.0% w/w of the skin wash composition. The amount of amphoteric 5 surfactant will to some extent be determined by the alkylpolyglucoside surfactant component of the detergent base.

Typically, the detergent base consisting of the mixture of non-ionic alkylpolyglucoside surfactant and amphoteric surfactant will constitute up to 30 10 %w/w of the skin wash composition. Suitably the detergent base will constitute from 5.0 to 20.0 %w/w and more suitably from 8.0 to 18.0 %w/w of the skin wash composition.

Control of pH to within defined limits is an essential feature of the present invention. 15 A pH within the desired range 3.0 to 4.5 is conferred partly by the inherent properties of the acid and specific surfactants and quantities thereof making up the detergent base and partly, where required, by use of a suitable neutralising agent for the acid. Any topically acceptable neutralising agent which is compatible with the other components of the composition can be used. It has been found that the neutralising 20 agent tromethamine is particularly suitable for skin wash compositions containing  $\alpha$ -hydroxy acids or other acids as defined herein. Other suitable neutralising agents include sodium hydroxide and triethanolamine. The amount of neutralising agent will be determined by the acid/base properties of the other ingredients which make up the composition and the pH selected for the composition.

25 The skin wash compositions of the invention may also contain additional topically acceptable skin conditioning and soothing agents, for example in the form of anti-inflammatory agents and vitamins or vitamin derivatives, typically at low concentrations, for example in the range 0.01 to 2.0 %w/w of the total composition. 30 Examples of topically acceptable anti-inflammatory agents include allantoin and

bisabolol. A preferred vitamin derivative is vitamin E acetate which has anti-inflammatory properties.

Additionally, compositions of the present invention will suitably contain

5 pharmaceutically and cosmetically acceptable additives or excipients conventional in the field of topical medicines and cosmetics, including for example thickeners, moisturisers, re-fattening agents, preservatives, conditioners, chelating agents, colouring agents, fragrances, UV filters and/or emulsifiers. The additives or excipients used in any given composition will be compatible both with each other and with the essential

10 ingredients of the composition such that there is no interaction which would impair the performance of the active ingredients. All additives or excipients must of course be non-toxic and of sufficient purity to render them suitable for human use.

Suitable thickeners include polymeric high molecular weight, non-ionic surfactants

15 consisting of a long chain (C<sub>12</sub> to C<sub>18</sub>) polyethylene glycol fatty acid or fatty acid residue. Examples include PEG 200 hydrogenated glyceryl palmitate, PEG 55 propylene glycol oleate, PEG 150 distearate and PEG 200 glycetyl tallowate. Suitable low molecular weight thickeners include cocamide DEA, laureth-3 and glycetyl monolaurate. A thickener comprising a polyurethane resin, propylene glycol and

20 water sold under the trade name Acrysol 44 also performs well in detergent base skin wash compositions. A thickener will suitably comprise up to 10.0 %w/w of the composition, more suitably from 2.0 to 5.0 %w/w. Preferred moisturisers include glycerin, propylene glycol, sorbitol and polyethylene glycol. A moisturiser may comprise up to 15%w/w of the composition, more generally from 2.0 to 6.0 %w/w of

25 the composition. Suitable re-fattening agents generally comprising 0.5 to 5.0 %w/w of the composition, preferably 0.75 to 2.0 %w/w include polyethylene glycol 7 and glycetyl cocoate. Suitable preservatives generally comprising 0.01 to 1.00 %w/w of the composition and suitably 0.10 to 0.30 %w/w, include phenoxyethanol and methyl dibromo glutaronitrile and mixtures thereof. Suitable conditioners, generally

30 comprising 0.1 to 5.0 %w/w of the composition and suitably 1.0 to 3.5%w/w include hydroxycetyl hydroxyethyl dimonium chloride and polyquaternium 39. Suitable

chelating agents, generally comprising up to 1.0 %w/w of the composition and suitably 0.1 to 0.3 %w/w include ethylene diamine tetra-acetic acid (EDTA), hydroethylene diamine triacetic acid (HEEDTA), diethylene triamine penta-acetic acid (DPTA) and cyclohexane diamine tetra-acetic acid (CTDA).

5

The balance of the composition is typically water and/or other non-alcohol solvent so as to make up 100 %w/w of the composition. The preferred solvent is water which will generally constitute more than 50 %w/w of the skin wash composition. Other suitable non-alcohol solvents which may be included to aid solution of the  $\alpha$ -hydroxy acid include glycols such as propylene glycol and macrogols.

The skin wash compositions of the invention may be prepared by methods well known in the art and readily available to the skilled formulator. Generally the acid and the surfactants making up the detergent base, together with any additives, are dissolved in solvent, the pH of the resulting mixture is checked and adjusted if appropriate and the viscosity of the composition is set to the desired level by addition of thickening agents. The present invention extends to a process for preparing a skin wash composition as hereinbefore defined comprising the admixture of the  $\alpha$ -hydroxy acid or other acid as defined herein with the detergent base in an aqueous solvent system and adjusting the pH as required such that the pH of the composition is in the range 3.0 to 4.5.

The present invention additionally encompasses the use of a skin wash composition as hereinbefore defined wherein the acid is salicylic acid for the manufacture of a medicament for the treatment and/or prophylaxis of acne. The use of compositions of the present invention as hereinbefore defined as a cosmetic treatment for improving the appearance and condition of human skin also forms part of the invention.

The following examples further describe and demonstrate compositions falling within the scope of the invention. For the avoidance of doubt, the examples are solely for the purpose of illustration and are not limiting with respect to the scope of the invention.

**Example 1 - Skin Wash Composition containing Lactic Acid**

A composition comprising the following ingredients was prepared. The resulting  
 5 composition had a pH of approximately 3.5.

<b>Ingredient</b>		<b>%w/w</b>
$\alpha$ -hydroxy acid :	lactic acid	1.0
detergent base :	decyl glucoside	3.5
10	lauryl glucoside	3.6
	cocoamidopropyl betaine	5.0
thickener :	PEG 120 methyl glucose dioleate	3.2
preservative :	phenoxyethanol	0.25
solvent :	water	to 100 %
15		

**Example 2 - Skin Wash Composition containing Salicylic Acid**

A composition comprising the following ingredients was prepared. The resulting composition was a clear product having a pH of 4.5.

<b>Ingredient</b>		<b>%w/w</b>
acid :	salicylic acid	2.0
detergent base :	lauryl glucoside	2.4
	decyl glucoside	2.0
25	cocamidopropyl betaine	2.8
neutralising agent :	Tromethamine	1.5
thickener :	PEG 120 methyl glucose dioleate	4.0
solvent :	de-ionised water	to 100 %
30		

**Example 3 - Skin Wash Composition containing Salicylic Acid**

The composition of Example 2 containing the additional excipients indicated below was prepared. The resulting clear product had a pH of 4.5.

5

conditioner	:	hydroxycetyl hydroxyethyl dimonium chloride
chelating agent	:	EDTA
preservative	:	phenoxyethanol
anti-inflammatory agent	:	allantoin & vitamin E acetate

## CLAIMS

1. A skin wash composition comprising from 0.1 to 10 %w/w of an  $\alpha$ -hydroxy acid or other acid as defined herein and a detergent base consisting of a mixture of a non-  
5 ionic alkylpolyglucoside surfactant and an amphoteric surfactant wherein the pH of the said composition is in the range 3.0 to 4.5.
- 10 2. A composition according to claim 1 wherein the acid is citric acid, malic acid, maleic acid, pyruvic acid, hydroxy-octanoic acid, salicylic acid, lactic acid or glycolic acid.
- 15 3. A composition according to claim 2 wherein the acid is salicyclic acid.
4. A composition according to claim 3 comprising from 0.2 to 5.0% w/w salicylic acid.
- 15 5. A composition according to claim 4 comprising 1.0 to 3.0% w/w salicylic acid.
- 20 6. A composition according to claim 2 wherein the  $\alpha$ -hydroxy acid is lactic acid which comprises from 0.1 to 5.0% w/w of the composition.
7. A composition according to claim 6 comprising from 0.5 to 2.5% w/w lactic acid.
- 25 8. A composition according to claim 2 wherein the  $\alpha$ -hydroxy acid is glycolic acid which comprises from 2.0 to 10.0% w/w of the composition.
9. A composition according to any one of claims 1 to 8 wherein the alkylpolyglucoside surfactant is decyl glucoside, lauryl glucoside or mixtures thereof.
- 30 10. A composition according to any one of claims 1 to 9 wherein the alkylpolyglucoside surfactant comprises up to 20% w/w of the said composition.
11. A composition according to claim 10 wherein the alkylpolyglucoside surfactant comprises from 2.0 to 15% w/w of the composition.
- 35 12. A composition according to any one of claims 1 to 11 wherein the amphoteric surfactant comprises at least one betaine.
13. A composition according to claim 12 wherein the betaine is cocoamidopropyl betaine.
- 40 14. A composition according to any one of claims 1 to 13 wherein the amphoteric surfactant comprises up to 10% w/w of the said composition.
- 45 15. A composition according to claim 14 wherein the amphoteric surfactant comprises from 2.0 to 8.0% w/w of the composition.

16. A composition according to any one of claims 1 to 15 wherein the detergent base comprises up to 30% w/w of the said composition.
- 5    17. A composition according to any one of claims 1 to 16 further comprising a neutralizing agent.
18. A composition according to claim 17 wherein the said neutralizing agent is tromethamine, sodium hydroxide or triethanolamine.
- 10    19. A composition according to any preceding claim substantially as described herein with reference to the examples.
20. A method for the preparation of a composition as defined in any of claims 1 to 19, which method comprises admixing the  $\alpha$ -hydroxy acid or other acid as defined herein with the detergent base in an aqueous solvent system and adjusting the pH as required.
- 15    21. A composition as defined in any one of claims 3 to 5 and 9 to 20 for use in the treatment and/or prophylaxis of acne.
- 20    22. Use of a composition as defined in any one of claims 3 to 5 and 9 to 20 in the manufacture of a medicament for use in the treatment and/or prophylaxis of acne.
23. A method of treatment and/or prophylaxis of acne which comprises the administration of an effective amount of a pharmaceutical composition as defined in any one of claims 3 to 5 and 9 to 20.
- 25    24. Use of a composition as defined in any one of claims 1 to 19 as a cosmetic treatment for improving the appearance and condition of human skin.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 97/02984A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61K7/48 A61K7/50

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 93 25650 A (HENKEL CORPORATION) 23 December 1993 see the whole document ---	1-24
A	DE 44 35 495 A (HENKEL) 11 April 1996 see tables 1,2 ---	1-24
A	DE 195 04 914 C (GOLDWELL) 16 November 1995 see examples 2-4 ---	1-24
A	WO 95 31962 A (GOJO INDUSTRIES) 30 November 1995 see claims 1,11-13; examples 8-40; tables 8,10 ---	1-24
A	DE 44 08 228 A (HENKEL) 14 September 1995 see example 4 ---	1-24
		-/-

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

\*Z\* document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 October 1997	31.10.97

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patenttaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epenl,  
Fax: (+31-70) 340-3016

Authorized officer

Fischer, J.P.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/02984

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 429 815 A (FARYNIARZ ET AL.) 4 July 1995 see the whole document ---	1-24
A	WO 96 02225 A (UNILEVER) 1 February 1996 see example 1 -----	1-24

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 97/02984

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim(s) 23  
is(are) directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 5.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest:-

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

Inte. onal Application No

PCT/EP 97/02984

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9325650 A	23-12-93	AU 4408893 A CA 2135641 A EP 0647262 A JP 7507833 T MX 9303569 A	04-01-94 23-12-93 12-04-95 31-08-95 29-04-94
DE 4435495 A	11-04-96	WO 9610558 A EP 0784609 A	11-04-96 23-07-97
DE 19504914 C	16-11-95	AT 155036 T AU 4445796 A CA 2169530 A DE 59600010 D EP 0727204 A FI 960654 A JP 8239312 A	15-07-97 22-08-96 16-08-96 14-08-97 21-08-96 16-08-96 17-09-96
WO 9531962 A	30-11-95	AU 2642195 A	18-12-95
DE 4408228 A	14-09-95	WO 9524377 A EP 0749413 A	14-09-95 27-12-96
US 5429815 A	04-07-95	CA 2145613 A EP 0676188 A JP 7277951 A	12-10-95 11-10-95 24-10-95
WO 9602225 A	01-02-96	AU 2934195 A CA 2190833 A US 5661189 A	16-02-96 01-02-96 26-08-97